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| 10/551,901   | 10/04/2005  | Hiroshi Miura        | 277987US0PCT        | 6206             |
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| EXAMINER   |             |                      |                     |                  |
| PALENIK, JEFFREY T   |             |                      |                     |                  |
| ART UNIT   |             | PAPER NUMBER         |                     |                  |
| 1615   |             |                      |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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**Office Action Summary****Application No.**

10/551,901

**Applicant(s)**

MIURA ET AL.

**Examiner**

Jeffrey T. Palenik

**Art Unit**

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 October 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,7 and 10-23 is/are pending in the application.
- 4a) Of the above claim(s) 14-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7 and 10-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 5 Oct 2010

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### **STATUS OF THE APPLICATION**

Receipt is acknowledged of Applicants' Request for Continued Examination (RCE), Amendments and Remarks, filed 5 October 2010, in the matter of Application N° 10/551,901. Said documents are entered on the record. The Examiner further acknowledges the following:

Claims 1, 7, and 10-23 are pending, where claims 14-23 remain withdrawn from consideration.

Claims 2-4 are newly cancelled.

Claim 1 has been amended to recite chemical compounds which define the porous silicon material. The claim has also been amended to recite that the composition is suitable for oral administration. Claims 7 and 10-12 have been amended to depend from claim 1. Independent 13 now recites that it comprises the composition of claim 1.

No new claims have been added.

The Examiner acknowledges that no new matter has been added to the claims.

Thus, claims 1, 7 and 10-13 now represent all claims currently under consideration.

### **INFORMATION DISCLOSURE STATEMENT**

One new Information Disclosure Statement (IDS) filed 5 October 2010 is acknowledged and has been considered.

#### **PRIORITY**

The present application is a national stage entry of PCT/JP04/06141 (WO 2004/096280) which was originally filed 28 April 2004. PCT/JP04/06141 further claims priority from US Provisional Application N° 60/466,069 filed 29 April 2003. The matter has been reconsidered by the Examiner. Applicants are granted an earliest effective U.S. filing date in accordance with the US Provisional Application which is determined to be 29 April 2003.

#### **WITHDRAWN REJECTIONS**

##### Rejection under 35 USC 102

The anticipation rejection previously made over claims 1, 7 and 13, under 35 USC §102(b), as discussed in the Advisory Action mailed 1 April 2010, is withdrawn. This was agreed upon in the interview held 10 March 2010 based on the discussion of the art and the Declarations filed. The rejection now stands **withdrawn**.

##### Rejection under 35 USC 103

Applicants' remarks presented in traversal of the obviousness rejections made to claims 1, 7 and 10-13, over Verhoff et al. alone or in combination with Yanaki et al. have been fully considered and are persuasive. Specifically, the remarks distinguish colloidal silica over the presently claimed forms, notably as the "colloidal" form is not known to be porous. Further the arguments that Verhoff provides a chemically-induced form of colloidal silica is also persuasively argued, namely because it is the coating applied to the

colloidal silica which is made porous rather than the silica itself. As such, the rejection now stands **withdrawn**.

#### **NEW OBJECTIONS/REJECTIONS**

In light of the aforementioned withdrawn rejections and the amended base claim, the following objection(s) and rejection(s) are presented:

#### **CLAIM OBJECTIONS**

Claim 1 is objected to because of the following informality: it contains an improper Markush group. From MPEP 2173.05(h): "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925)...It is improper to use the term "comprising" instead of "consisting of." *Ex parte Dotter*, 12 USPQ 382 (Bd. App. 1931)". In the instant case, Applicants recite that "the porous silicon material comprises light anhydrous silicic acid, hydrated silicon dioxide, silicon dioxide or calcium sulfate".

Appropriate correction is required.

#### **CLAIM REJECTIONS - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The properties of the “porous silicon material” as recited in lines 12-17 of the claim, appear to conflict, thereby rendering the invention indefinite. On one hand, the “porous silicon material is not a porous silica material having an average pore diameter of 1 to 20 nm” whereas line 17 states that “the porous silicon material has an average pore diameter of 1 to 500 nm”. Claim 7 further recites that the average pore diameter range is 2 to 200 nm.

Clarification is respectfully requested.

#### **CLAIM REJECTIONS - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 7 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Akiyama et al. (US Pre-Grant Publication N° 2004/0058956) in further view of Yanaki et al. (USPN 5,538,728; already of record) and further evidenced Iwahashi et al. (EP 1 323 786).**

The instant invention is drawn to a composition comprising a very low water-soluble drug and a porous silicon material; said material is defined further as being light anhydrous silicic acid, hydrated silicon dioxide, silicon dioxide or calcium sulfate. Applicants' claimed embodiments are interpreted in light of the instant disclosure (MPEP §2111) as also being defined by their trademarks (e.g., Sylaysia<sup>®</sup>). Thus, regarding the dimensional limitation(s) recited in claim 1, pertaining to the porous silicon material; until some material difference(s) in the properties of the composition are demonstrated, said limitation is considered by the Examiner to be directed toward the composition, which is

instantly claimed. That is, a showing in the art of the claimed composition will be interpreted by the Examiner as reading on Applicants' claimed compounds.

Akiyama et al. teach pharmaceutical compositions comprising a water-poorly soluble or insoluble HER2 inhibitory substance, wherein the solubility in water of the substance is improved (Abstract; claim 1). Claim 8 further discloses that such a substance will have a solubility of less than 10 mg/mL at 25°C. Paragraphs [0341] and [0342] disclose and define other hormone therapeutic agents which may be used by the invention of Akiyama for the same purpose (i.e., improving solubility). Solid dispersions of the invention are disclosed as being prepared as well as orally administrable to humans ¶[0356]. Said dispersions are further disclosed as containing additives which are preferably taught as including calcium silicate (e.g., Florite-RE) and light silicic anhydride (e.g., Sylysia) ¶¶[0302]-[0304]. Thus the limitations of claims 1, 7, 10 and 13 are considered to have been met by the reference. The limitations of claim 11 are considered to be read upon by ¶[0328] which states that the preferable weight ratio of the additive such as an excipient (e.g., Florite or Sylysia) to a water-poorly soluble substance is usually in the range of 0.1:1 to 20:1, preferably 0.3:1 to 10:1 and more preferably 1:1 to 3:1.

While Akiyama does disclose that the water-poorly soluble substance whose solubility is improved, is preferably HER2 inhibitory substance, it is expressly disclosed that other substances possessing said property may be delivered from the dosage forms disclosed. One such active ingredient is prednisolone. However, the reference does not specifically disclose using prednisolone valerate acetate, per the instant claim 12. Yanaki remedies this deficiency.



Yanaki et al. teach a pharmaceutical dosage forms comprising a complexation of a water-swellaable silicate mineral and a drug (claims 12 and 1). Said water-swellaable silicate material is taught as including silicon dioxide (col. 4, lines 15-20). The active pharmaceutical ingredients used in the invention while not particularly limited, are generally taught as including a steroid hormone such as prednisolone valerate acetate, for instance where the application applies to rectal administration (col. 10, lines 40-45).

A person of ordinary skill in the art, would have been motivated to prepare the instantly claimed composition, at the time of the instant invention. Applicants' claimed method limitations set forth in claim 1, wherein the composition is produced by treating a mixture comprising the low water-soluble drug and the porous silicon material with a super- or subcritical carbon dioxide fluid are considered, in light of MPEP §2113, to be immaterial. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) In the instant case, both Akiyama and Yanaki teach dosage forms which result in the instantly claimed composition wherein the respective purpose of each teaching is to improve the solubility of active ingredients which are naturally poorly-soluble in water. As discussed above, any showing of the porous silica material in the art would be considered by the Examiner to teach the instantly

claimed limitations, absent a clear showing of evidence to the contrary. In the instant case, Akiyama teaches the use of Sylysia light anhydrous silicic acid. This teaching is considered to meet the recited properties limitations as evidenced by the discussion of the properties by Iwashashi et al. (EP 1 323 786). Herein it is disclosed that Sylysia is used to prepare a silica hydrogel having a specific surface area of 285 m<sup>2</sup>/g and a pore volume.

Lastly, it is apparent that one of ordinary skill in the art would have had clear motivation to modify Akiyama such that it would improve the delivery of prednisolone valerate acetate from its formulations. "The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)" "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.) See MPEP 2144.07.

Thus, based on the combined guidance of the references, the ordinarily skilled artisan would have had a reasonably high expectation in successfully producing the instantly claimed composition. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, alone or in combination, especially in the absence of evidence to the contrary.

All claims have been rejected; no claims are allowed.

**CORRESPONDENCE**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/  
Examiner, Art Unit 1615

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